

WHAT IS CLAIMED IS:

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1. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
  - 5 (a) the nucleotide sequence as set forth in SEQ ID NO: 1 or SEQ ID NO: 4;
  - (b) the nucleotide sequence of the DNA insert in ATCC Deposit Nos. PTA-1753 or PTA-1755;
  - (c) a nucleotide sequence encoding the polypeptide as set forth in SEQ  
10 ID NO: 2 or SEQ ID NO: 5;
  - (d) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a) - (c); and
  - (e) a nucleotide sequence complementary to any of (a) - (c).
- 15 2. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
  - (a) a nucleotide sequence encoding a polypeptide that is at least about 70 percent identical to the polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5 wherein the encoded polypeptide has an activity of the polypeptide set  
20 forth in SEQ ID NO: 2 or SEQ ID NO: 5;
  - (b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in SEQ ID NO: 1 or SEQ ID NO: 4, the nucleotide sequence of the DNA insert in ATCC Deposit Nos. PTA-1753 or PTA-1755, or (a);
  - 25 (c) a region of the nucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 4, the DNA insert in ATCC Deposit Nos. PTA-1753 or PTA-1755, (a), or (b) encoding a polypeptide fragment of at least about 25 amino acid residues wherein the polypeptide fragment has an activity of the encoded polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5, or is antigenic;

(d) a region of the nucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 4, the DNA insert in ATCC Deposit Nos. PTA-1753 or PTA-1755, or any of (a) - (c) comprising a fragment of at least about 16 nucleotides;

(e) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a) - (d); and

(f) a nucleotide sequence complementary to any of (a) - (d).

3. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

10 (a) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5 with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5;

15 (b) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5 with at least one amino acid insertion, wherein the encoded polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5;

20 (c) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5 with at least one amino acid deletion, wherein the encoded polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5;

25 (d) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5 which has a C- and/or N- terminal truncation, wherein the encoded polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5;

30 (e) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the encoded polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5;

(f) a nucleotide sequence of any of (a) - (e) comprising a fragment of at least about 16 nucleotides;

(g) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a) - (f); and

5 (h) a nucleotide sequence complementary to any of (a) - (e).

4. A vector comprising the nucleic acid molecule of Claims 1, 2, or 3.

5. A host cell comprising the vector of Claim 4.

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6. The host cell of Claim 5 that is a eukaryotic cell.

7. The host cell of Claim 5 that is a prokaryotic cell.

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8. A process of producing a Secs-1 polypeptide comprising culturing the host cell of Claim 5 under suitable conditions to express the polypeptide, and optionally isolating the polypeptide from the culture.

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9. A polypeptide produced by the process of Claim 8.

10. The process of Claim 8, wherein the nucleic acid molecule comprises promoter DNA other than the promoter DNA for the native Secs-1 polypeptide operatively linked to the DNA encoding the Secs-1 polypeptide.

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11. The isolated nucleic acid molecule according to Claim 2 wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

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12. A process for determining whether a compound inhibits Secs-1 polypeptide activity or Secs-1 polypeptide production comprising exposing a cell

according to Claims 5, 6, or 7 to the compound and measuring Secs-1 polypeptide activity or Secs-1 polypeptide production in said cell.

5 13. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as set forth in SEQ ID NO: 2 or SEQ ID NO: 5; and

(b) the amino acid sequence encoded by the DNA insert of ATCC Deposit Nos. PTA-1753 or PTA-1755.

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14. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as set forth in SEQ ID NO: 3 or SEQ ID NO: 6, optionally further comprising an amino-terminal methionine;

15 (b) an amino acid sequence for an ortholog of SEQ ID NO: 2 or SEQ ID NO: 5;

(c) an amino acid sequence that is at least about 70 percent identical to the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 5 wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 2 or  
20 SEQ ID NO: 5;

(d) a fragment of the amino acid sequence set forth in SEQ ID NO: 2 or SEQ ID NO: 5 comprising at least about 25 amino acid residues wherein the fragment has an activity of the polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5, or is antigenic; and

25 (e) an amino acid sequence for an allelic variant or splice variant of the amino acid sequence as set forth in SEQ ID NO: 2 or SEQ ID NO: 5, the amino acid sequence encoded by the DNA insert of ATCC Deposit Nos. PTA-1753 or PTA-1755, or any of (a) - (c).

30 15. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as set forth in SEQ ID NO: 2 or SEQ ID NO: 5 with at least one conservative amino acid substitution, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5;

5 (b) the amino acid sequence as set forth in SEQ ID NO: 2 or SEQ ID NO: 5 with at least one amino acid insertion, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5;

(c) the amino acid sequence as set forth in SEQ ID NO: 2 or SEQ ID NO: 5 with at least one amino acid deletion, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5;

(d) the amino acid sequence as set forth in SEQ ID NO: 2 or SEQ ID NO: 5 which has a C- and/or N- terminal truncation, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5; and

15 (e) the amino acid sequence as set forth in SEQ ID NO: 2 or SEQ ID NO: 5 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 2 or SEQ ID NO: 5.

20 16. An isolated polypeptide encoded by the nucleic acid molecule of Claims 1, 2, or 3.

17. The isolated polypeptide according to Claim 14 wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

18. An antibody produced by immunizing an animal with a peptide comprising an amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 5.

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19. An antibody or fragment thereof that specifically binds the polypeptide of Claims 13, 14, or 15.

20. The antibody of Claim 19 that is a monoclonal antibody.

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21. A hybridoma that produces a monoclonal antibody that binds to a peptide comprising an amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 5.

22. A method of detecting or quantitating the amount of Secs-1 polypeptide using the anti-Secs-1 antibody or fragment of Claims 18, 19, or 20.

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23. A selective binding agent or fragment thereof that specifically binds at least one polypeptide wherein said polypeptide comprises the amino acid sequence selected from the group consisting of:

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(a) the amino acid sequence as set forth in SEQ ID NO: 2 or SEQ ID NO: 5; and

(b) a fragment of the amino acid sequence set forth in SEQ ID NO: 2 or SEQ ID NO: 5; or a naturally occurring variant thereof.

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24. The selective binding agent of Claim 23 that is an antibody or fragment thereof.

25. The selective binding agent of Claim 23 that is a humanized antibody.

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26. The selective binding agent of Claim 23 that is a human antibody or fragment thereof.

27. The selective binding agent of Claim 23 that is a polyclonal antibody or fragment thereof.

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28. The selective binding agent Claim 23 that is a monoclonal antibody or fragment thereof.

5 29. The selective binding agent of Claim 23 that is a chimeric antibody or fragment thereof.

30. The selective binding agent of Claim 23 that is a CDR-grafted antibody or fragment thereof.

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31. The selective binding agent of Claim 23 that is an antiidiotypic antibody or fragment thereof.

32. The selective binding agent of Claim 23 which is a variable region fragment.

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33. The variable region fragment of Claim 32 which is a Fab or a Fab' fragment.

20 34. A selective binding agent or fragment thereof comprising at least one complementarity determining region with specificity for a polypeptide having the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 5.

35. The selective binding agent of Claim 23 which is bound to a detectable label.

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36. The selective binding agent of Claim 23 which antagonizes Secs-1 polypeptide biological activity.

37. A method for treating, preventing, or ameliorating a Secs-1 polypeptide-related disease, condition, or disorder comprising administering to a patient an effective amount of a selective binding agent according to Claim 23.

5 38. A selective binding agent produced by immunizing an animal with a polypeptide comprising an amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 5.

39. A hybridoma that produces a selective binding agent capable of  
10 binding a polypeptide according to Claims 1, 2, or 3.

40. A composition comprising the polypeptide of Claims 13, 14, or 15 and a pharmaceutically acceptable formulation agent.

15 41. The composition of Claim 40 wherein the pharmaceutically acceptable formulation agent is a carrier, adjuvant, solubilizer, stabilizer, or anti-oxidant.

42. The composition of Claim 40 wherein the polypeptide comprises  
20 the amino acid sequence as set forth in SEQ ID NO: 3 or SEQ ID NO: 6.

43. A polypeptide comprising a derivative of the polypeptide of Claims 13, 14, or 15.

25 44. The polypeptide of Claim 43 which is covalently modified with a water-soluble polymer.

45. The polypeptide of Claim 44 wherein the water-soluble polymer is selected from the group consisting of polyethylene glycol, monomethoxy-polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene  
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glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide copolymers, polyoxyethylated polyols, and polyvinyl alcohol.

46. A composition comprising a nucleic acid molecule of Claims 1, 2,  
5 or 3 and a pharmaceutically acceptable formulation agent.

47. A composition of Claim 46 wherein said nucleic acid molecule is  
contained in a viral vector.

10 48. A viral vector comprising a nucleic acid molecule of Claims 1, 2,  
or 3.

49. A fusion polypeptide comprising the polypeptide of Claims 13, 14,  
or 15 fused to a heterologous amino acid sequence.

15 50. The fusion polypeptide of Claim 49 wherein the heterologous  
amino acid sequence is an IgG constant domain or fragment thereof.

51. A method for treating, preventing or ameliorating a medical  
20 condition comprising administering to a patient the polypeptide of Claims 13, 14,  
or 15 or the polypeptide encoded by the nucleic acid of Claims 1, 2, or 3.

52. The method of Claim 51 wherein the medical condition being  
treated, prevented, or ameliorated is a hematopoietic disorder, osteoporosis,  
25 osteopetrosis, osteogenesis imperfecta, Paget's disease, periodontal disease,  
hypercalcemia, acute glomerulonephritis, chronic glomerulonephritis, cancer,  
diabetes, obesity, or cachexia.

53. A method of diagnosing a pathological condition or a susceptibility  
30 to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of Claims 13, 14, or 15, or the polypeptide encoded by the nucleic acid molecule of Claims 1, 2, or 3 in a sample; and

5 (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

54. A device, comprising:

(a) a membrane suitable for implantation; and

10 (b) cells encapsulated within said membrane, wherein said cells secrete a protein of Claims 13, 14, or 15; and

said membrane is permeable to said protein and impermeable to materials detrimental to said cells.

15 55. A method of identifying a compound which binds to a polypeptide comprising:

(a) contacting the polypeptide of Claims 13, 14, or 15 with a compound; and

20 (b) determining the extent of binding of the polypeptide to the compound.

56. The method of Claim 55 further comprising determining the activity of the polypeptide when bound to the compound.

25 57. A method of modulating levels of a polypeptide in an animal comprising administering to the animal the nucleic acid molecule of Claims 1, 2, or 3.

30 58. A transgenic non-human mammal comprising the nucleic acid molecule of Claims 1, 2, or 3.

59. A process for determining whether a compound inhibits Secs-1 polypeptide activity or Secs-1 polypeptide production comprising exposing a transgenic mammal according to Claim 58 to the compound, and measuring Secs-1 polypeptide activity or Secs-1 polypeptide production in said mammal.